

Comparison of FIB-4 and APRI in HIV-HCV Coinfected Patients With Normal and Elevated ALT

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Background

- HCV has a more progressive course in HIV-HCV coinfecting patients
 - Assessing liver disease severity is even more important in this population
- Liver biopsy remains the gold standard for assessment of disease severity in patients with chronic HCV and HIV-HCV coinfection
 - Unfortunately, there are significant cost and risks associated with this procedure
- Noninvasive models have been developed as an alternative
 - Many use tests not routinely available to the clinician
 - Others, including FIB-4 and APRI, utilize routine tests

Background (cont)

- The FIB-4 and APRI have already been validated as useful screening tests in coinfecting patients
 - Most cohorts only included patients with elevated ALT
- However, a significant proportion of patients with HCV have normal ALT
 - Therefore, validation of these models are needed in those with normal ALT

Aims

- To validate both FIB-4 and APRI in *all* HIV-HCV coinfecting patients
 - Specifically, in patients stratified by normal and elevated ALT

Methods

- Study design
 - Prospective cross-sectional analysis
- Study participants
 - HIV-HCV coinfecting patients seen at Virginia Commonwealth University Health System in Richmond, Virginia between 1994 and 2008
- All data were collected at time of biopsy

Methods: Inclusion Criteria

- Inclusion criteria
 - HIV infection
 - Positive antibody
 - HCV infection
 - Positive HCV RNA

Methods: Exclusion Criteria

- Exclusion criteria
 - Hepatic decompensation
 - Ascites, INR >1.5, PSE
 - Elevated creatinine (>2.0 mg/dL)
 - HBV surface antigen positive
 - Evidence of another liver disease
 - Autoimmune hepatitis
 - α -1 anti-trypsin deficiency
 - Hereditary hemochromatosis
 - Wilson Disease

Methods: Equations

- **FIB-4**

$$= \frac{\text{Age} \times \text{AST}}{\text{PLT} \times \text{ALT}^{1/2}}$$

- Cutoffs: ≤ 1.45 or ≥ 3.25

- **APRI**

$$= \frac{(\text{AST}/\text{ULN}) \times 100}{\text{PLT}}$$

- Cutoffs: ≤ 0.5 or ≥ 1.5

*Normal ALT: ≤ 60 U/L in men, ≤ 50 in women
ULN AST: 50*

Methods

- Histology was assessed for Ishak score
- Performance of each assay and ROC curves for predicting advanced fibrosis (Ishak 4-6) were calculated for the entire group and those with and without normal ALT

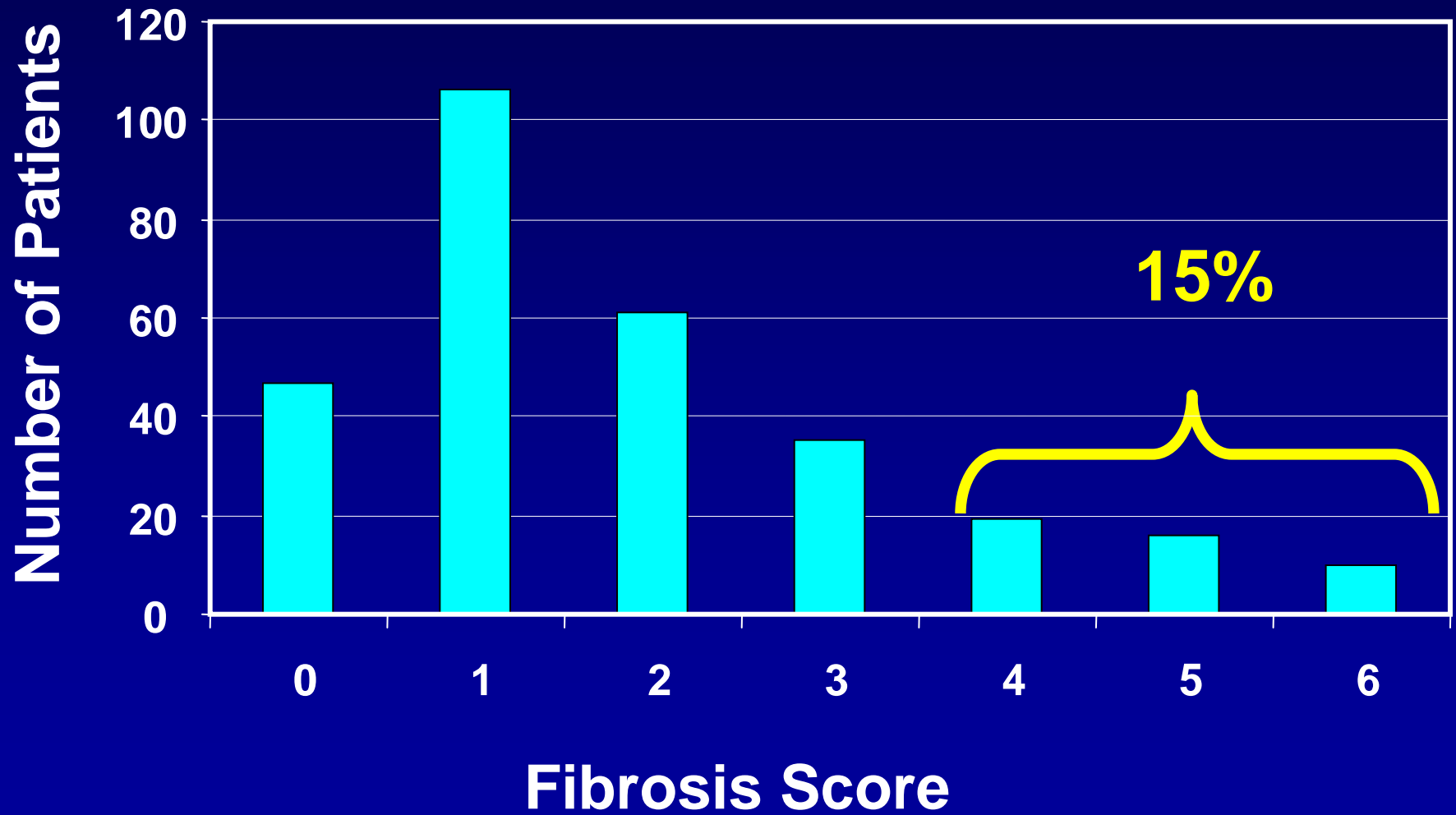
Patient Characteristics

N	298
Age (years)	46 ± 8
Gender (% male)	74
Race (% African American)	80
HAART use (%)	84
NRTI (%)	100
NNRTI (%)	60
PI (%)	47
CD4 (μ/L)	525 ± 318
HIV Viral Load <400 (%)	53
HCV Genotype 1 (%)	92

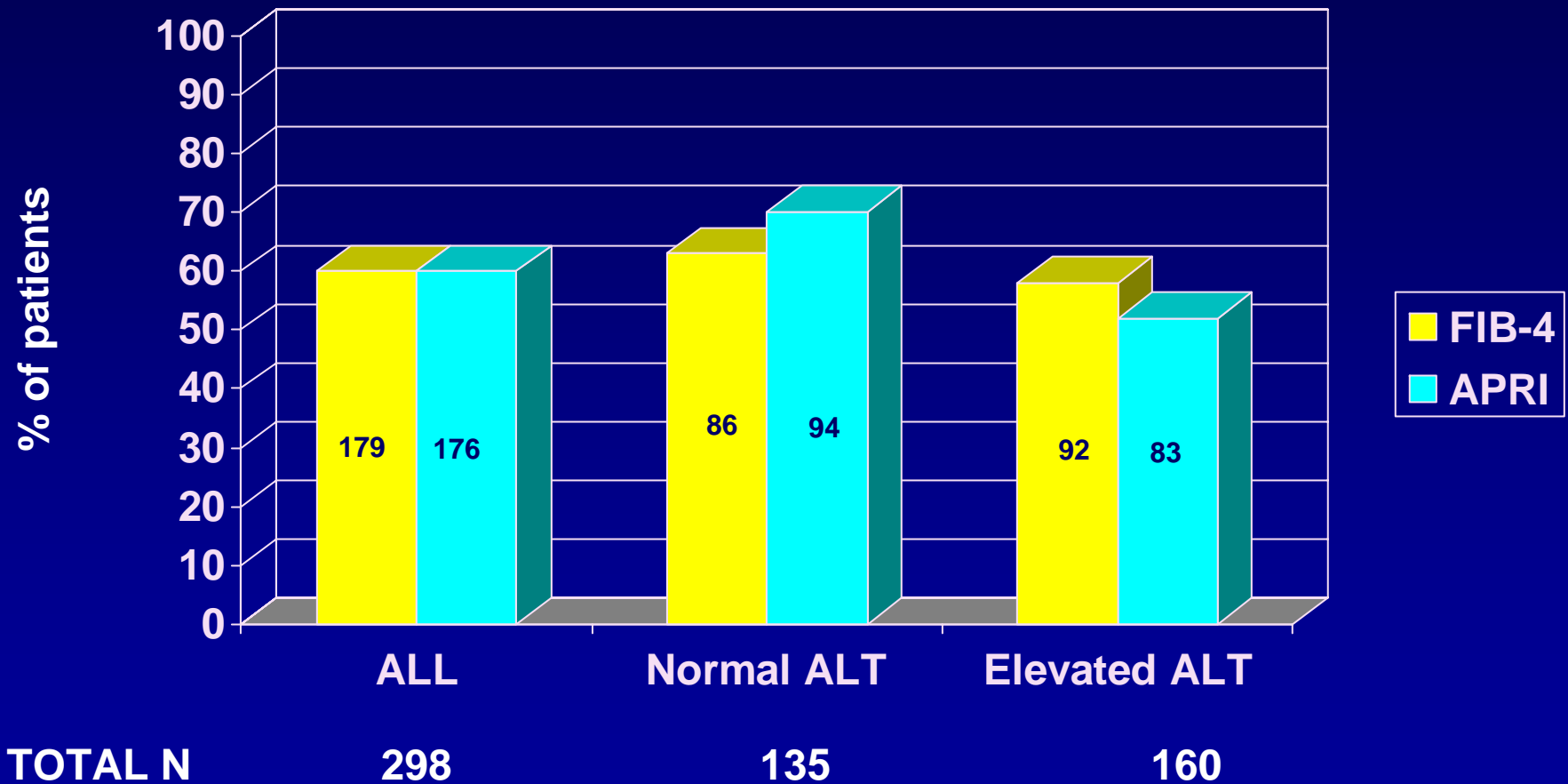
Patient Characteristics (cont)

AST (U/L)	85 ± 70
ALT (U/L)	83 ± 66
PLT (x 10⁹)	208 ± 76
Elevated ALT (%)	55
Inflammation score	6.4 ± 2.5
Periportal	2.0 ± 1.0
Lobular	2.1 ± 1.1
Portal	2.3 ± .85
Fibrosis score	1.5 ± 1.1
Advanced fibrosis (%)	15
Liver biopsy length	20.5 ± 8.3 mm

Distribution of Ishak Fibrosis Scores



Proportion of patients with Determinant Values

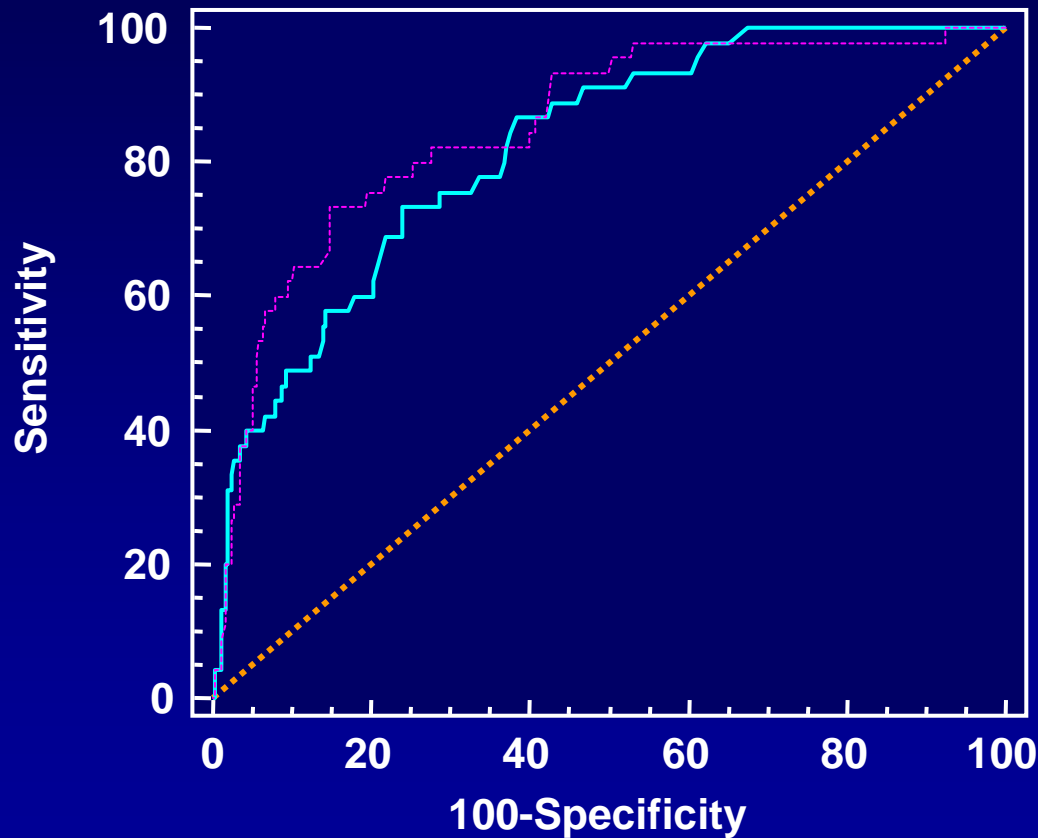


Performance of the Models

		Sen	Spec	PPV	NPV	Accuracy
Total						
(n=179)	FIB-4	.97	.78	.47	.99	.81
(n=176)	APRI	.88	.78	.41	.97	.79
Normal ALT						
(n=86)	FIB-4	1.0	.91	.50	1.0	.91
(n=94)	APRI	.67	.99	.67	.99	.97
Elevated ALT						
(n=92)	FIB-4	.96	.62	.46	.98	.71
(n=83)	APRI	.91	.45	.39	.93	.58

ROC: FIB-4 and APRI

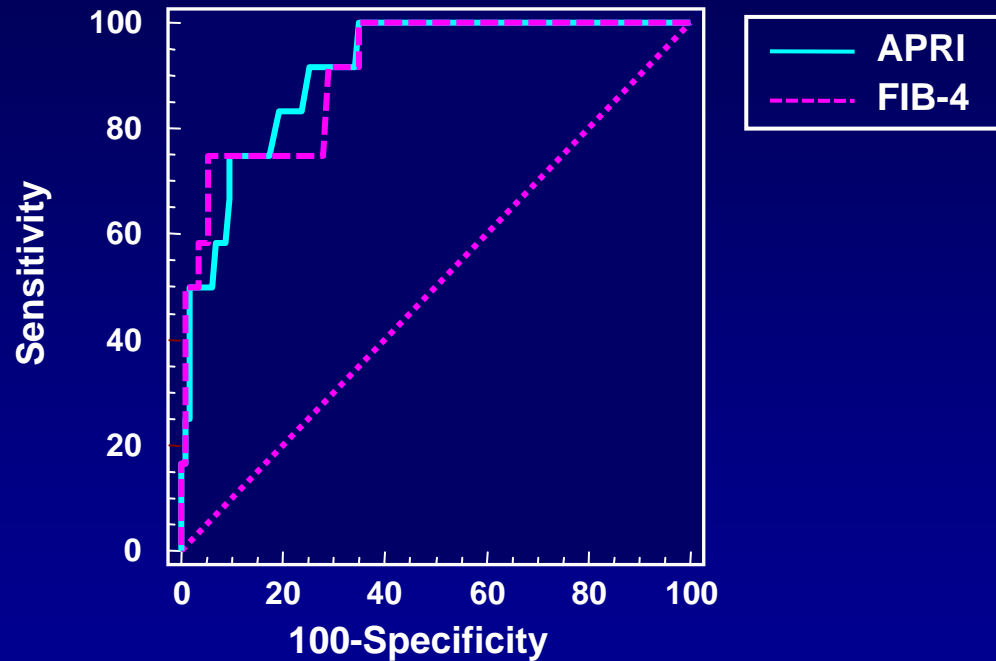
All Patients



	AUC	95% CI
APRI	0.82	0.77 to 0.86
FIB-4	0.85	0.81 to 0.89

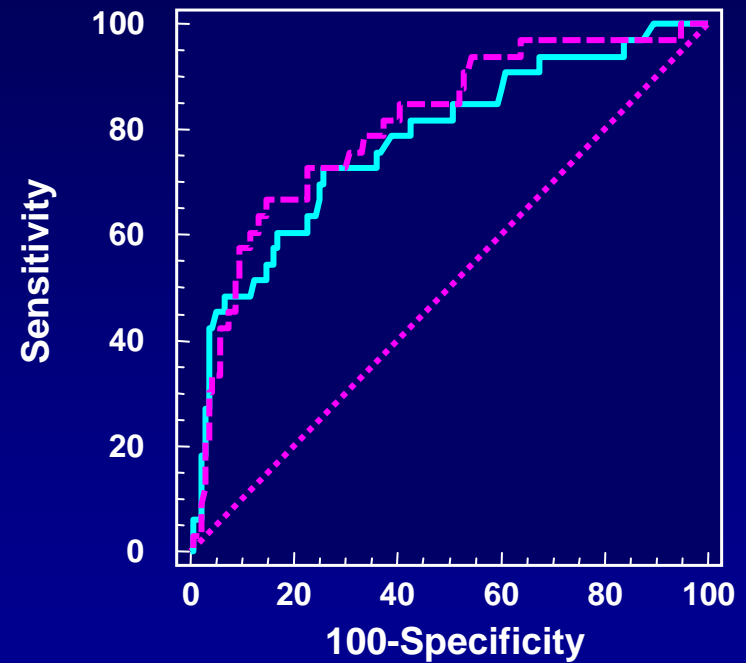
ROC: FIB-4 and APRI

Normal ALT



	AUC	95% CI
APRI	0.90	0.85 to 0.95
FIB-4	0.90	0.84 to 0.95

Elevated ALT



	AUC	95% CI
APRI	0.76	0.70 to 0.84
FIB-4	0.80	0.74 to 0.86

Discordant Results

	FIB-4		APRI	
	≤ 1.45 Inappropriately classified as 0-3	≥ 3.25 Inappropriately classified as 4-6	$\leq .5$ Inappropriately classified as 0-3	≥ 1.5 Inappropriately classified as 4-6
Normal ALT	0%	50%	2%	32%
Elevated ALT	2%	54%	7%	60%

Summary

- Both models performed well, especially in those with normal ALT
- In those with elevated ALT, FIB-4 performed better than APRI
- The high negative predictive value of excluding advanced fibrosis was slightly better using FIB-4
- Neither model had a high positive predictive value for advanced fibrosis

Conclusions

- Ideally, a noninvasive marker would identify both patients with significant fibrosis at risk for progression, decompensation and HCC, as well as identify those patients with little or no fibrosis, who may not benefit from HCV therapy
- However, because of their moderate PPV, liver biopsy may still be required patients who have $\text{FIB-4} \geq 1.45$ or $\text{APRI} \geq .5$
- The tradeoff of increasing the upper cutoff values for either test is improved PPV and accuracy versus increased proportion of patients with indeterminate values. Thus, the overall need for liver biopsy may not change